claim 13 tracks claim 3, new claim 14 tracks claim 4, new claim 15 tracks claim 2, new claim 16 tracks claim 3, new claim 17 tracks claim 4, new claim 18 tracks claim 8.

I. Informality and Sequence Listing Objections

The Specification and Sequence Listing are amended to comply with the informalities referred to by the Examiner, including the addition of an Abstract of the Invention, "SEQ ID NO:" references, and replacement of brackets ("[" and "]" with "{" and "}" respectfully) such that there is no confusion whether the terms inside the curved brackets (*i.e.*, {S-Acm}) are included in the peptide sequence. It is respectfully submitted that the Substitute Specification and amended Sequence Listing are in condition for allowance.

Claims 4-8 stand objected to under 37 C.F.R. § 1.75(c) as being in improper form as a multiple dependent claim cannot depend from another multiple dependent claim. The amendments to claims 4-8 overcome this objection. This objection should therefore be withdrawn.

II. Rejection under 35 U.S.C. § 112, ¶1

Claims 1-3 stand rejected under 35 U.S.C. § 112, first paragraph. The Examiner has indicated that the specification, while being enabling for a peptide obtained from amino acid residues 33-42 of murine epidermal growth factor ($mEGF_{(33-42)}$) wherein the peptide is modified to protect it from proteolytic degradation, binds to laminin receptors and has substitution of Tyr by Tic-OH or of Arg by citrulline, does not reasonably provide enablement for a peptide derived from $mEGF_{(33-42)}$ wherein the peptide is modified to protect it from proteolytic degradation, binds to laminin receptors and has substitution of Tyr by any Tyr analog or substitution of Arg by any Arg analog. This rejection is overcome for the following reasons.

The enablement requirement is satisfied if the specification describes any method for making and using the claimed invention that bears a "reasonable correlation" to the entire scope of the claims. *In re Fisher*, 427 F.2d 833, 839 (C.C.P.A. 1970) (copy attached). The patent application need not contain within its four corners all of the information necessary to practice the claimed invention. M.P.E.P. § 2164.05(a). Information that was well known to persons of ordinary skill in the art need not be included in the application, and preferably is omitted. *In re Buchner*, 929 F.2d 660 (Fed. Cir. 1991) (copy attached). The Examiner points to the eight *Wands* factors in the enablement rejection, but only three of the eight factors are construed against Applicants. It is respectfully submitted that the eight factors considered ***as a group***, as required by *Wands*, clearly shows the claims and specification of the instant application are enabled as written. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (copy attached).

The Examiner's attention is respectfully directed to page 2, line 15 to page 4, line 32 of the Substitute Specification where support for determining each of the Tyr and Arg analogs is provided. Within this section, conformational restriction, three-dimensional predictive strategies, and molecular dynamics modelling is described. Analogues such as Tic-OH, 2', 6'-dimethyl-beta-methyl-tyrosines, 2-O-methyl and 2-O-ethyl-tyrosine, α, α-dialkyl substituted amino acids such as α-amino isobutyric acid and aminocyclopropane acid and the like are specifically mentioned. Further, there are many other well-known ways in the art to modify the peptide residues to protect the modified murine epidermal growth factor peptide from proteolysis. Examples include the use of D-amino acids, reduced peptide bond isosteres (methylene-amino), sulphonepeptides, unnatural amino acid analogues and the like. Four examples on page 4, lines 13-32 of the Substitute Specification are provided enabling those skilled in the art to modify the peptide without undue experimentation to discover all of the Tyr and Arg analogues claimed in the application.

The Examiner has also indicated it is not apparent from the specification how the binding activity of the peptide resulting from the modification of the sequence is predicted. Applicants assert that a screening method well-known to a person skilled in the art could have been used at the time of the invention to assess the binding activity of modified peptides toward laminin receptors. This screening method includes synthesizing 67LR ligands with either a radioactive, fluorescent or biotin label (each peptide being tested for receptor binding, agonism and antagonism of laminin and EGF using methods described in the specification). Next, unpurified native recombinant or His-tagged 67LR is coated onto 96-well plates using established procedures and biotin- or fluorescently-labeled peptide ligands are applied (a "total-binding" procedure). Specificity of binding is monitored by inclusion of saturating amounts of unlabelled $mEGF_{(33-42)}$ (or laminin) to a parallel set of incubations (a "non-specific binding" procedure). After incubation and washing, 67LR binders are revealed by application of steptavidin enzyme conjugate (alkaline phosphatase or peroxidase) and incubation with substrate. The presence of a coloured product is indicates binding of a labeled ligand to the immobilised receptor. Using fluorescently-labeled peptide ligands, fluorescent positive wells with no fluorescence in the matching "non-specific binding." Non-specific binders are fluorescence in both sets; non-binders are blank in both sets. Binding affinity of binders identified above are determined by displacement of labeled $mEGF_{(33-42)}$ from solid-phase 67LR either on 67LR-coated microtitre plates or His-tagged 67LR immobilised on Biacore biosensor chips with detection by surface plasmon resonance detection. This protocol for determining the binding activity of each of the modified peptides was well-known in the art at the time of the invention.

Although Applicants assert that the instant invention is enabled without undue experimentation, even a "considerable amount" of experimentation is permissible in a patent application if it is merely routine or if the specification provides a reasonable amount of

guidance. M.P.E.P. § 2164.05. It is submitted that the specification enables any person skilled in the art to make and use a murine epidermal growth factor peptide comprising any Tyr or Arg analogue. It is further submitted that the specification enables any person skilled in the art to make and use the methods of treating various disease states mediated by laminin receptor binding using the entire range of modified peptide factors. Therefore, one skilled in the art would clearly be able to practice the method of amended claims 1-8 and additional claims 9-18 without undue experimentation using the specification as a guide. Accordingly, it is respectfully requested that the rejection of claims 1-4 under 35 U.S.C. §112, first paragraph, be withdrawn.

III. Rejection under 35 U.S.C. § 112, ¶2

Claims 1-3 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. It is respectfully submitted that the amendments to claims 1-3 overcome this rejection. This rejection should therefore be withdrawn.

IV. Conclusion

Accordingly, Applicants respectfully submit that independent claims 1, 5 and 6 are allowable over the prior art of record. For similar reasons, Applicant urges that the dependent claims are also allowable.

All stated grounds of objection and rejection have been properly accommodated or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance as all patentability requirements have been met.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, he is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment is respectfully requested.

Respectfully submitted,

Kevin W. Buckley, Esq.
U.S.P.T.O. Reg. No. 45,901
Attorney for Applicants

Thompson Coburn LLP
One US Bank Plaza
St. Louis, MO 63101
314.552.6350
314.552.7350 facsimile

Attachments:
1. A marked up version of the Substitute Specifications
2. Clean form without markings of the Substitute Specifications
3. Clean form without markings of pending claims
4. *In re Fisher*, 427 F.2d 833, 839 (C.C.P.A. 1970)
5. *In re Buchner*, 929 F.2d 660 (Fed. Cir. 1991)
6. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988)
7. Sequence Listing

*929 F.2d 660, *; 1991 U.S. App. LEXIS 4775, **;*
18 U.S.P.Q.2D (BNA) 1331

IN re JOHANNES B. BUCHNER

No. 91-1046

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

929 F.2d 660; 1991 U.S. App. LEXIS 4775; 18 U.S.P.Q.2D (BNA) 1331

March 26, 1991, Decided

PRIOR HISTORY:

[1]** Appealed from U.S. Patent and Trademark Office; Board of Patent Appeals and Interferences.

DISPOSITION: Affirmed.

CASE SUMMARY

PROCEDURAL POSTURE: Petitioner appealed from U.S. Patent and Trademark Office Board of Patent Appeals and Interferences ruling that denied his patent request.

OVERVIEW: The claimed invention related to a higher order digital transmission system which communicated a plurality of separate digital streams over a common channel. The application was rejected by the Patent and Trademark Office (PTO) on the ground that it failed to describe how to make and use the phase comparator and divider without undue experimentation. The examiner asserted that the comparator was not a typical two input phase comparator and the divider was not a typical one input divider. Petitioner offered a declaration that stated the elements referred to in the application were well-known to those of ordinary skill in the art as of the filing date of a foreign priority application. The PTO rejected the offer of proof. The Board on appeal affirmed. The court also affirmed stating that an expert's opinion on the ultimate issue must be supported by more than a conclusory statement.

OUTCOME: The court affirmed the agency's denial of the patent application because the petitioner failed to meet the burden of proof to support his claim.

CORE TERMS: comparator, divider, examiner, phase, declaration, well-known, invention, routinely, input, built, disclosure, affirming, skill, well known, patent, disclose, enabling, skilled, filing date, unsupported, conclusory, overcoming, declarant, receiver, digital, output, block

CORE CONCEPTS - ♦ Hide Concepts

Patent Law : Specification & Claims : Definiteness
Patent Law : Specification & Claims : Enablement Requirement
In order to be enabling under 35 U.S.C.S. § 112, a patent application must sufficiently disclose an invention to enable those skilled in the art to make and use it. The specification need not disclose what is well known in the art. However, an examiner

may reject a claim if it is reasonable to conclude that one skilled in the art would be unable to carry out the claimed invention.

Patent Law : Specification & Claims : Definiteness
Patent Law : Specification & Claims : Enablement Requirement
Patent Law : Specification & Claims : Description Requirement
35 U.S.C.S. § 112 requires that, unless the information is well known in the art, the application itself must contain this information; it is not sufficient to provide it only through an expert's declaration.

Evidence : Witnesses : Expert Testimony
An expert's opinion on the ultimate legal issue must be supported by something more than a conclusory statement.

COUNSEL: Jack E. Haken, U.S. Philips Corporation, of Tarrytown, New York, submitted for Appellant.

Fred E. McKelvey, Solicitor, Office of the Solicitor, of Arlington, Virginia, submitted for Appellee. With him on the brief were Richard E. Schafer and Lee E. Barrett, Associate Solicitors.

JUDGES: Mayer, Michel, and Lourie, Circuit Judges.

OPINIONBY: LOURIE

OPINION: [*660] LOURIE, Circuit Judge

Johannes B. Buchner appeals from the July 17, 1990, decision of the Board of Patent Appeals and Interferences (Board), Appeal No. 89-2590, affirming the examiner's rejection of all of his claims for failure to provide an enabling disclosure under the first paragraph of 35 U.S.C. § 112. We affirm.

BACKGROUND

The claimed invention relates to a higher order digital transmission system which communicates a plurality of separate digital streams over a common channel. It includes a transmitter portion (block encoding arrangements and multiplexer) and receiver portion (a demultiplexer and block decoding arrangements). The receiver portion of the system further includes a phase comparator having four inputs and one output and a divider having two inputs **[**2]** and one output.

Buchner's application was rejected by the Patent and Trademark Office (PTO) on the ground that it failed to describe how to make and use the phase comparator and divider without undue experimentation. Although the functions of the phase comparator **[*661]** and divider were adequately disclosed, the examiner rejected the application because the design structures of the two elements were not disclosed. The examiner asserted that the comparator was not a typical two input phase comparator and the divider was not a typical one input divider.

Buchner offered a declaration of Professor Jan Louis de Kroes which stated that "the elements referred to in the application as divider 19 and phase comparator 16 were well-known to those of ordinary skill in the art as of June 17, 1985," the filing date of a foreign priority application. The declaration also stated that these elements were "routinely built"; it provided details concerning the structure and function of the elements.

The PTO did not accept the declaration as overcoming the rejection, stating that it was mere conclusion unsupported by factual documentation and that it provided inadequate indication that the technology concerning **[**3]** the comparator and divider was well-known.

The Board, on all the evidence before it, found that there was a reasonable basis for the examiner to question the sufficiency of the disclosure with respect to the structure of the comparator and divider and that the declarant's assertions that these elements were "well-known" and "routinely built" were conclusory statements unsupported by any other evidence.

DISCUSSION

Buchner claims that the Board erred in affirming the examiner's rejection, arguing that the declaration of de Kroes, an expert, unequivocally establishes a fact that cannot be dismissed "in the absence of a . . . contrary inference from other evidence." We affirm the Board's decision.

In order to be enabling under 35 U.S.C. § 112, a patent application must sufficiently disclose an invention to enable those skilled in the art to make and use it. The specification need not disclose what is well known in the art. *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 U.S.P.Q. (BNA) 481, 489 (Fed. Cir. 1984). However, an examiner may reject a claim if it is reasonable to conclude that one skilled in the art would be unable **[**4]** to carry out the claimed invention. *See In re Eynde*, 480 F.2d 1364, 1370, 178 U.S.P.Q. (BNA) 470, 474 (CCPA 1973).

We conclude that it was reasonable in this case for the examiner to doubt that the claimed invention could have been carried out based on the disclosure since the elements at issue are integral to the practice of the invention and neither the application nor the prior art describe their structure. The applicant thus had the burden of overcoming this rejection. *Id.*

The declaration of de Kroes did provide significant detail concerning the structure and function of the elements in question. However, § 112 requires that, unless the information is well known in the art, the application itself must contain this information; it is not sufficient to provide it only through an expert's declaration. *In re Smyth*, 38 C.C.P.A. 1130, 189 F.2d 982, 990, 90 U.S.P.Q. (BNA) 106, 112) (1951).

Moreover, an expert's opinion on the ultimate legal issue must be supported by something more than a conclusory statement. *See In re Brandstadter*, 484 F.2d 1395, 1405, 179 U.S.P.Q. (BNA) 286, 294 (CCPA 1973). De Kroes only stated that "the elements **[**5]** referred to in the application as divider 19 and phase comparator 16 were well known to those of ordinary skill in the art as of June 17, 1985" and that they were "routinely built." He did not provide adequate support for his conclusion. What he did described was how *he* would construct the divider and phase comparator, but he did not demonstrate that such construction was well-known to those of ordinary skill in the art.

As stated by the Board, "if the relatively complex phase comparator and divider arrangement described in the declaration were so 'well-known' and 'routinely built' as of the effective filing date, the declarant should have [had] no trouble documenting the same. . . ."

[*662] We conclude that the Board did not err in affirming the examiner's rejection of all the claims in Buchner's application for failure to comply with 35 U.S.C. § 112, paragraph 1.

AFFIRMED

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*57 C.C.P.A. 1099, *; 427 F.2d 833, **;*
*1970 CCPA LEXIS 345, ***; 166 U.S.P.Q. (BNA) 18*

IN RE JOSEPH D. FISHER

No. 8208

United States Court of Customs and Patent Appeals

57 C.C.P.A. 1099; 427 F.2d 833; 1970 CCPA LEXIS 345; 166 U.S.P.Q. (BNA) 18

Oral argument November 6, 1969 June 11, 1970

PRIOR HISTORY: [*1]**

Appeal from Patent Office, Serial No. 72,481

DISPOSITION: Affirmed.

CASE SUMMARY

PROCEDURAL POSTURE: Appellant sought review of decision of Patent Office Board of Appeals, which affirmed rejection of remaining two claims in appellant's application for "Adrenal Gland Stimulating Concentrate and Method for the Preparation Thereof," which was continuation in part of prior application that had been previously before the court.

OVERVIEW: Appellant sought review of the patent office decision, which rejected remaining two claims in appellant's application for preparation of substances containing adrenocorticotrophic hormones in composition suitable for injection into human beings in treatment of arthritis and other conditions. The application was continuation in part of prior application that had been previously before the court. The claims had been rejected by the patent office on grounds of res judicata, because substances had been anticipated by previously granted patents, for indefiniteness, and for insufficient disclosure under 35 U.S.C.S. § 112. The court held that res judicata did not apply because different issue was presented in later proceeding and claims should not have been rejected for indefiniteness. The court also held, however, that subject matter was anticipated by prior patents, and appellant could not rely on filing date of parent specification because parent did not adequately describe substances; and that rejection for insufficient disclosure was proper, and affirmed rejection of claims.

OUTCOME: The decision of the patent office board of appeals, which rejected two remaining claims in appellant's application was affirmed because subject matter of application was anticipated by previous patents and application disclosed insufficient information to support claims, although board's rejection on additional grounds of res judicata and indefiniteness was incorrect.

CORE TERMS: sequence, amino acids, potency, specification, disclosure, recited, examiner, composition, milligram, preparation, chemical, indefiniteness, indefinite, beef, hog, discloses, tyrosine, gland, recitation, vasopressin, pituitary, oxytocin, extract, chain, amino acid, inherently, breadth, polypeptide, teaching, hormone

CORE CONCEPTS - ◆ Hide Concepts

Patent Law : Novelty & Anticipation

Patent Law : Specification & Claims : Definiteness

The use of new expressions is allowed when they are definite, and Patent Office may call for comparative evidence when there is reason to believe that the prior art discloses matter that renders the claimed subject matter old or obvious.

Patent Law : Specification & Claims : Enablement Requirement

The first paragraph of 35 U.S.C.S. § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

COUNSEL: *Carl C. Batz, Frank T. Barber,* attorneys of record, for appellant. *George R. Jones, Robert H. Berdo, Beale and Jones,* of counsel.

Joseph Schimmel for the Commissioner of Patents. *Jack E. Armore,* of counsel.

OPINIONBY: LANE

OPINION: [834]**

[*1100] Before Rich, Almond, Baldwin, Lane, Associate Judges, and Matthews, Judge, sitting by designation.

Lane, Judge, delivered the opinion of the court:

This appeal is from the decision of the Patent Office Board of Appeals, which affirmed the rejection of claims 4 and 5, the only claims remaining in appellant's application serial No. 72,481, filed November 29, 1960, for Adrenal Gland Stimulating Concentrate and Method for the Preparation Thereof. The application is a continuation-in-part of a prior co-pending application serial No. 435,451, filed June 9, 1954, which was before this court in In re Fisher, 50 CCPA 1025, 307 F.2d 948, 135 USPQ 22 (1962). That application was a continuation of application serial No. 122,588, filed October 20, 1949, which we shall refer to as the parent application.

The Disclosure

The instant specification relates **[***2]** to the preparation of substances containing adrenocorticotrophic hormones (ACTH) in a composition suitable for injection into human beings in the treatment of certain forms of arthritis and other human pathological conditions. It is stated that previous ACTH products were unsatisfactory for administration to humans because of their low potency, generally around **[*1101]** 50% of "International Standard," and because of their relatively high content of undesirable factors, notably posterior pituitary hormones which consent mainly of oxytocic and vasopressor principles. A method n1 is disclosed for producing ACTH preparations having potencies ranging from 111% to 230% of standard and containing no more than 0.08 units of vasopressin and no more than 0.05 units of oxytocin per International Unit of ACTH, which limits are said to be tolerable to humans. The method generally starts with frozen pituitary glands of hogs, sheep, beef or other animals, including whales. These glands are quick-thawed in an organic solvent to extract

contaminated ACTH from the gland meat. A precipitate containing the active material is recovered, free of contaminants, by treatment with fractionating salts. **[***3]** The material is then subjected to hydrolysis, and an inactive fraction of hydrolized fragmented material is separated from a fraction containing the active substance. The active fraction is then adjusted to a pH above 2.8, the excess salts being separated from the concentrate of the active principle. Several variations of this procedure are set forth and six specific examples are given. The specification then states that the ACTH concentrate produced as described is found to contain peptides having free amino and carboxyl groups, and is further characterized:

n1 The method is said to be covered by appellant's patent 3,192,115, issued June 29, 1965.

by its solubility in glacial acetic acid and phenol; by its relative insolubility in other organic solvents; by its greater stability under acid conditions than under alkali conditions; by its susceptibility to attack by proteolytic enzymes and peptidases; and by its positive reaction to the Millon and xanthoproteic tests for tyrosine, the biuret test for peptide linkage, the ninhydrin test for free amino groups in the alpha position, the Sakaguchi test for guanidine groups, and the Hopkins-Gole and benzaldehyde tests for indole **[***4]** nuclei and tryptophane.

The specification then states that the product can be characterized structurally as a peptide containing a chain of identifiable amino acids. While the exact sequence will vary from product to product, depending on the source and preparative history of the product, the first 24 **[**835]** amino acids in the chain, counting from the N terminus of the molecule, will have the following sequence: (1) Serine, (2) Tyrosine, (3) Serine, (4) Methionine, (5) Glutamic Acid, (6) Histadine, (7) Phenylalanine, (8) Arginine, (9) Tryptophan, (10) Glycine, (11) Lysine, (12) Proline, (13) Valine, (14) Glycine, (15) Lysine, (16) Lysine, (17) Arginine, (18) Arginine, (19) Proline, (20) Valine, (21) Lysine, (22) Valine, (23) Tyrosine, (24) Proline. ACTH obtained from hogs contains a sequence of 39 amino acids, the first 24 being as recited above; ACTH obtained from sheep or beef also contains a sequence of 39 amino acids, the first 24 being as recited, and the 25th to **[*1102]** 39th being in a sequence different from that of the hog extract. n2 No structural description is given for ACTH extracted from other animals.

n2 The 25-to-39 sequence for sheep is set forth, but for beef the sequence is apparently unknown. It is stated that the empirical formula for beef and sheep ACTH is the same. **[***5]**

The Claims

Appellant defines the subject matter sought to be patented as follows:

4. An adrenocorticotrophic hormone preparation containing at least 1 International Unit of ACTH per milligram and containing no more than 0.08 units of vasopressin and no more than 0.05 units of oxytocin per International Unit of ACTH, and being further characterized as containing as the active component of [a?] polypeptide of at least 24 amino acids having the following sequence from the N terminus of the molecule; Serine, Tyrosine, Serine, Methionine, Glutamic Acid, Histadine, Phenylalanine, Arginine, Tryptophan, Glycine, Lysine, Proline, Valine, Glycine, Lysine, Lysine, Arginine, Arginine, Proline, Valine, Lysine, Valine, Tyrosine, Proline.

5. An adrenocorticotrophic hormone preparation containing at least 1 International Unit of ACTH per milligram and containing no more than 0.08 units of vasopressin and no more than 0.05 units of oxytocin per International Unit of ACTH, and being further characterized by its solubility in glacial acetic acid and phenol; by its relative insolubility in other organic solvents; by its greater stability under acid conditions than under alkali conditions; **[***6]**

by its susceptibility to attack by proteolitic enzymes and peptidases; and by its positive reaction to the Millon and xanthoproteic tests for tyrosine, the biuret test for peptide linkages, and the ninhydrin test for free amino groups in the alpha position, the Sakaguchi test for guanidine groups, and the Hopkins-Gole and benzaldehype tests for indole nuclei and tryptophane.

Opinion

There are many grounds of rejection affirmed by the board in this case. We shall set them forth separately, with our opinion on each.

(a) The res judicata rejection

[1] The board affirmed the examiner's rejection of claim 5 on the ground of res judicata, stating that the claim differed from claim 13 in Fisher, supra, "mainly in calling for a 'preparation containing at least 1 Interational Unit of ACTH per milligram' in place of the terminology in claim 13 'concentrate having a potency at least equal to that of the International Standard.'" The board held this to be "no significant difference other than in verbiage." We reverse the board on this ground of rejection. "Verbiage" was the very problem in Fisher. The court there found that the words "a potency at least equal to the International **[***7]** Standard" rendered the claims unpatentable under the second paragraph of 35 USC 112. 50 CCPA at 1029, 307 F.2d **[*1103]** at 950-51, 135 USPQ at 24. These words do not appear in the claims before us. Thus, a different issue is presented and res judicata does not apply. See In re Fried, 50 CCPA 954, 312 F.2d 930, 136 USPQ 429 (1963). **[**836]**

(b) The rejection on the Li references

The examiner rejected claim 4 under 35 USC 102 as anticipated by the following references:

Li et al. (III), Science, vol. 124, p. 934 (Nov. 9, 1956).

Li et al., J.A.C.S., vol. 80, No. 10, pp. 2587-88 (May 20, 1958).

Appellant did not contest the pertinence of these references, but sought to remove them by relying on his parent application which, as mentioned above, was filed in 1949. The examiner took the position that appellant was not entitled to the parent date under 35 USC 120 because the parent contained insufficient disclosure to support claim 4 in the manner required by the first paragraph of 35 USC 112. The board affirmed this rejection for two reasons. First, since the parent application lacked any structural description of the ACTH extracts therein disclosed, the board concluded **[***8]** that it could not be determined whether those products would meet the terms of claim 4, which recites a specific sequence of the first 24 amino acids. Appellant contended that the parent application inherently disclosed products meeting the terms of claim 4, even though appellant did not know the chemical structure of those products when the parent application was filed. Appellant cited several cases in support of the proposition that inherent disclosure is sufficient under 35 USC 112, including Riester v. Kendall, 34 CCPA 859, 159 F.2d 732, 72 USPQ 481 (1947), and In re Nathan, 51 CCPA 1059, 328 F.2d 1005, 140 USPQ 601 (1964). The board did not dispute the correctness of this proposition, but found that "it has not been established that the parent disclosures inherently produce the claimed products * * *." We agree with appellant that this finding was erroneous. The parent application discloses treatment of hog pituitary extracts. The Li (J.A.C.S.) article discloses the amino acid sequence for beef ACTH and states that the first 24 amino acids in the sequence are the same for porcine (hog) ACTH, namely, the sequence recited in claim 4. The hog-extracted products disclosed in **[***9]** appellant's parent application must therefore have had the recited sequence. The board's second reason for holding the parent application insufficient to support claim 4 was that the products

disclosed in the parent were insufficient to support a claim of the breadth of claim 4. On this point we agree with the board. The claim recites that the product must contain "at least" 24 amino acids in a specified sequence. The parent disclosure mentions treating extracts from "hog, beef, lamb, and other animal pituitary glands, and including also pituitary **[*1104]** glands of whales." From the instant specification and the Li articles, we know that hog, beef and lamb ACTHs will contain 39 amino acids, of which the first 24 will be in the recited sequence. We do not know, from the record, the chemical structure of ACTHs of whales or other animals. Appellant's parent application, therefore, discloses no products, inherently or expressly, containing other than 39 amino acids, yet the claim includes all polypeptides, of the recited potency and purity, having at least 24 amino acids in the chain in the recited sequence. The parent specification does not enable one skilled in the art to **[***10]** make or obtain ACTH's with other than 39 amino acids in the chain, and there has been no showing that one of ordinary skill would have known how to make or obtain such other ACTH's without [2] undue experimentation. As for appellant's conclusion that the 25th to 39th acids in the chain are unnecessary, it is one thing to make such a statement when persons skilled in the art are able to make or obtain ACTH having other than 39 amino acids; it is quite another thing when they are not able to do so. In the latter situation, the statement is in no way "enabling" and hence lends no further support for the broad claim. We conclude that appellant's parent application is insufficient to support a claim as broad as claim 4. For this reason we affirm the board's rejection of claim 4 as unpatentable over the Li references. **[**837]**

(c) The rejection on Collip

The examiner rejected both claims under 35 USC 102 as unpatentable over Collip, "Properties of Anterior Lobe Extracts," Symposia Quant. Biol., vol. 5, pp. 210-12 (1937). The examiner's position was that, although Collip does not expressly anticipate the claims, Collip and appellant prepare their ACTH under identical conditions, **[***11]** and it follows that the products produced are identical. The board noted that Judge Smith's dissenting opinion in Fisher, supra, expressed the view that Collip did not render similar product claims obvious under 35 USC 103. The majority in Fisher did not reach that issue. The board here concluded, however, that the examiner's rejection on Collip under 35 USC 102 was correct. The board stated: "Since the claim terminology is not sufficiently definite to positively distinguish over the products inherently produced by following the Collip disclosure, this rejection will be sustained." Appellant contends, and we agree, that Collip is deficient in so many material respects that it cannot be reasonably concluded that it discloses anything like the compositions here claimed. There is substantial doubt as to whether Collip uses a pH less than 3.0. The doubt arises because the pH at the origin of a Collip graph of pH vs. weight of adrenals is not indicated by a numeral. The solicitor contends that this point represents a pH of 1.0. **[*1105]** Appellant contends that it is merely a control point, and supports this contention by observing that controls are stated on the graph and that, **[***12]** if a pH of less than 3.0 were actually used, an increase of activity should result, as taught by appellant, rather than a decrease as indicated by the Collip graph. Further, as pointed out by Judge Smith, Collip describes experiments on rats and guinea pigs, and there is no indication that the vasopressin and oxytocin levels in the Collip products were within the safe-for-humans levels which are recited in the claims and which are an important aspect of appellant's contribution to the art. In view of these deficiencies, we believe appellant was not obliged to present comparative evidence to rebut the Patent Office position on the inherent disclosure of Collip. We reverse the board's affirmance of the rejections on Collip.

(d) The indefiniteness rejection

The examiner rejected both claims for indefiniteness under the second paragraph of 35 USC 112. He stated:

Claim 4 is indefinite in not setting forth the entire composition chemically. It would appear

that the amino acid sequence is only part of the chemical structure of the composition. Claims 4 and 5 are indefinite in not setting forth with particularity the chemical structure or adequate physical characteristics to identify **[***13]** the composition. * * *.

The board affirmed the indefiniteness rejection and gave reasons in addition to those stated by the examiner. We find that the claims before us are in compliance with the second paragraph of section 112 and that the board's affirmance of the indefiniteness rejection must be reversed. We shall discuss each reason given by the board.

[3] The board first found that some of the issues were the same as those treated by the board in the earlier Fisher case involving appellant's earlier application. The board here quoted several pages from its earlier opinion, the gist of which appears to be that the claims there involved, which recited no chemical structure, were indefinite in that potency and purity limitations there recited were inadequate to enable a decision to be made as to patentability over the prior art. The criticism of the use of the word "potency" was affirmed by this court in Fisher, supra. The word does not appear in the claims before us. The relevance of the quoted portion of the board's earlier opinion therefore appears to be with regard to the expression appearing in the present claims: "Containing at least 1 International Unit of ACTH **[***14]** per milligram **[**838]** and containing no more than 0.08 units of vasopressin and no more than 0.05 units of oxytocin per International Unit of ACTH." The specification states that "International Standard" means the generally accepted standard adopted by The Technical **[*1106]** Advisory Committee to the Study Section for Metabolism and Endocrinology of the National Institutes of Health, and that one milligram of the standard equals one International Unit. We fail to see anything indefinite in such a recitation. We recognize a problem in determining differences over the prior art where the claim uses language which is now accepted and precise but which was not used in the art at the time the prior-art references were published. However, were we to require that claims speak in the language of the prior art, we would be prohibiting the use of the newer and frequently more precise language of the present art. We think that the proper solution to this problem is to allow the use of new expressions when they are definite, and to allow the Patent Office, as it has always done, to call for comparative evidence when there is reason to believe that the prior art discloses matter which **[***15]** renders the claimed subject matter old or obvious.

[4] The board next agreed with the examiner that "the claims are so broad as to be indefinite in that they do not positively identify the entire chemical structure of the compound desired to be claimed." The board noted that claim 4 recited only a portion of the molecule, namely at least 24 amino acids in a certain sequence, "which does not describe adequately the products formed in appellant's specification." Here the examiner and the board have viewed the absence of a limitation as to amino acids beyond the 24th position as rendering the claim indefinite. While the absence of such a limitation obviously broadens the claim and raises questions of sufficiency of disclosure, it does not render the claim indefinite. The absence of the limitation has a precise meaning. Regardless of the specification, the claimed subject matter is in no way limited by the presence, absence or sequence of amino acids beyond the 24th position. This principle is the very basis of this court's consistent refusal to read limitations of the specification into the claims. See In re Prater, 56 CCPA 1381, 415 F.2d 1393, 162 USPQ 541 (1969), and cases **[***16]** therein cited. In our recent decision in In re Wakefield, 57 CCPA 959, 422 F.2d 897, 164 USPQ 636 (1970), we considered an indefiniteness rejection involving the absence of a limitation. We reversed the rejection, stating: "The scope of the claim is still definite, however, because each recited limitation is definite."

The board also found indefiniteness in the fact that the claims were not limited to compositions disclosed or suggested by appellant's specification, and would cover "a host of materials produced in any possible manner, including synthetically, which are neither taught nor represented by the specific materials actually formed in appellant's examples." Appellant

does not dispute that the claims are as broad as the board indicated. This fact, however, while very important **[*1107]** in assessing the sufficiency of appellant's disclosure to see if it will support such broad coverage, is entirely irrelevant to the issue of definiteness, for the reasons stated in the preceding paragraph.

We conclude that the board's affirmance of the rejection of the claims for indefiniteness under the second paragraph of 35 USC 112 must be reversed.

(e) The rejection for insufficient **[***17]** disclosure

The examiner did not reject the claims for insufficient disclosure. This was first applied by the board, although the board failed to denominate it a new ground of rejection under Rule 196 (b). Appellant apparently did not complain of such failure, but chose to appeal here.

The board stated:

[We] consider appellant's claims to be so broad that * * * the specification lacks sufficient supporting description to comply with the requirements of 35 USC 112, first **[**839]** paragraph. The board noted that the claims cover:

substantially all "preparations" produced synthetically or by breakdown of the 39 amino acid polypeptides in any manner to from a polypeptide product of lesser molecular weight containing any number (claim 5) or at least 24 (claim 4) of the amino acids as long as the product exhibits, without the stated side effects, activity equal to at least 1 International Unit of ACTH per milligram.

We have already discussed, with respect to the parent application, the lack of teaching of how to obtain other-than-39 amino acid ACTHs. That discussion is fully applicable to the instant application, and we think the board was correct in finding insufficient **[***18]** disclosure due to this broad aspect of the claims.

The second aspect of breadth mentioned by the board in the quoted portion of its opinion has not yet been discussed. This is the problem arising from the potency recitation "at least 1 International Unit of ACTH per milligram." This is a so-called "open-ended" recitation. It has a lower limit but no upper limit. As previously mentioned, the specification discloses products having potencies from 111% to 230% of standard, which we understand to mean from 1.11 to 2.30 International Units of ACTH activity per milligram. The issue thus presented is whether an inventor who is the first to achieve a potency of greater than 1.0 for certain types of compositions, which potency was long desired because of its beneficial effect on humans, should be allowed to dominate all such compositions having potencies greater than 1.0, including future compositions having potencies far in excess of those obtainable from his teachings plus ordinary skill.

[*1108] [5] It is apparent that such an inventor should be allowed to dominate the future patentable inventions of others where those inventions were based in some way on his teachings. **[***19]** Such improvements, while unobvious from his teachings, are still within his contribution, since the improvement was made possible by his work. It is equally apparent, however, that he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence not in compliance with the first paragraph of 35 USC 112. That paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies

inversely with the degree of unpredictability of the factors involved. In the present case we must conclude, on the record before us, that appellant has not enabled the preparation of ACTHs having potencies much greater than **[***20]** 2.3, and the claim recitations of potency of "at least 1" render the claims insufficiently supported under the first paragraph of 35 USC 112.

Our conclusion is in no way opposed to the principles of the cases cited by appellant in support of his contention that he is entitled to coverage of the breadth now sought. Farbenfabriken of Elberfeld Co. v. Kuelmsted ("the aspirin case"), 171 Fed. 887 (N.D. Ill. 1909), affd. 179 Fed. 701 (7th Cir. 1910), In re Williams, 36 CCPA 756, 171 F.2d 319, 80 USPQ 150 (1948), and Parke, Davis & Co. v. Mulford & Co., 196 Fed. 496 (2d Cir. 1912), each involved claims to substantially pure compositions. Such claims do not present the same breadth problem as here, because in those cases the possible range of further purification was either small or nonexistent. Such claims have an inherent upper limit of **[**840]** 100% purity, whereas in the present case it would appear theoretically possible to achieve potencies far greater than those obtained by appellant. Merck & Co. v. Olin Mathieson Chemical Corp., 253 F.2d 156, 116 USPQ 484 (4th Cir. 1958), involved a claim reciting an activity of "at least 440 L.L.D. units per milligram," but no issue appears **[***21]** to have been raised regarding that recitation and the court's opinion does not consider it.

For the reasons given above, the decision of the board is affirmed.

*858 F.2d 731, *; 1988 U.S. App. LEXIS 13208, **;*
8 U.S.P.Q.2D (BNA) 1400

In re JACK R. WANDS, VINCENT R. ZURAWSKI, JR., and HUBERT J. P. SCHOEMAKER

No. 87-1454

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

858 F.2d 731; 1988 U.S. App. LEXIS 13208; 8 U.S.P.Q.2D (BNA) 1400

September 30, 1988, Decided

SUBSEQUENT HISTORY: [1]**

As Amended October 20, 1988.

PRIOR HISTORY:

Appealed from: Patent and Trademark Office, Board of Patent Appeals and Interferences.

CASE SUMMARY

PROCEDURAL POSTURE: Appellant sought review of the decision of the Patent and Trademark Office Board of Patent Appeals and Interferences affirming rejection of appellant's application for a patent under 35 U.S.C.S. § 112 because appellant's written specifications would not enable a person to practice the claimed invention without undue experimentation.

OVERVIEW: Appellants contended that their written specifications fully enabled the practice of their claimed invention in accordance with 35 U.S.C.S. § 112 because the antibodies needed to perform the immunoassays could be made from readily available starting materials using methods that were well known in the antibody art. Respondent alleged that appellant's data presented that the production of antibodies was unpredictable and unreliable and that it would require undue experimentation for one skilled in the art to make the antibodies. The court agreed with appellant, holding that respondent's interpretation of the data was erroneous. Appellant's written disclosure fully enabled the claimed invention. Respondent's classification of the stored cell lines as failures was strained and unduly harsh. Appellant's explanation of its initial failures was reasonable and in view of the fact that the following six fusions were successful, the court concluded that appellant effectively rebutted respondent's challenge to 35 U.S.C.S. § 112.

OUTCOME: The court reversed the decision affirming rejection of appellant's application, concluding that appellant's written specification would not require undue experimentation to obtain antibodies needed to practice the claimed invention in order to meet the enablement requirement.

CORE TERMS: antibody, cell, hybridoma, invention, experimentation, antigen, affinity, undue, binding, monoclonal antibodies, patent, fusion, deposit, lymphocyte, high-affinity, screening, immunoassay, enablement, constant, isotype, specification, determinant, clone, experiment, monoclonal antibody, myeloma, bind, disclosure, stored, cpm

CORE CONCEPTS - ◆ Hide Concepts

Patent Law : Specification & Claims : Definiteness
Patent Law : Specification & Claims : Enablement Requirement
The first paragraph of 35 U.S.C.S § 112 requires that the specification of a patent must enable a person skilled in the art to make and use the claimed invention. Patents are written to enable those skilled in the art to practice the invention.

Patent Law : Specification & Claims : Enablement Requirement
Patent Law : Specification & Claims : Description Requirement
A patent need not disclose what is well known in the art.

Civil Procedure : Appeals : Standards of Review : Clearly Erroneous Review
Civil Procedure : Appeals : Standards of Review : De Novo Review
Although the court reviews underlying facts found by the board under a clearly erroneous standard, it reviews enablement as a question of law.

Patent Law : Specification & Claims : Enablement Requirement
Although inventions involving microorganisms or other living cells often can be enabled by a deposit, a deposit is not always necessary to satisfy the enablement requirement. No deposit is necessary if the biological organisms can be obtained from readily available sources or derived from readily available starting materials through routine screening that does not require undue experimentation.

Patent Law : Specification & Claims : Enablement Requirement
Whether the specification in an application involving living cells is enabled without a deposit must be decided on the facts of the particular case.

Patent Law : Specification & Claims : Enablement Requirement
Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is "undue", not "experimentation."

Patent Law : Specification & Claims : Enablement Requirement
The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

Patent Law : Specification & Claims : Enablement Requirement
Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations.

Patent Law : Specification & Claims : Enablement Requirement
Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth

of the claims.

COUNSEL: Jorge A. Goldstein, of Saidman, Sterne, Kessler & Goldstein, of Washington, District of Columbia, argued for Appellant. With him on the brief was Henry N. Wixon.

John H. Raubitschek, Associate Solicitor, Commissioner of Patents and Trademarks, of Arlington, Virginia, argued for Appellee. With him on the brief were Joseph F. Nakamura, Solicitor and Fred E. McKelvey, Deputy Solicitor.

JUDGES: Smith, Newman, and Bissell, Circuit Judges. Newman, Circuit Judge, concurring in part, dissenting in part.

OPINIONBY: SMITH

OPINION: [*733] SMITH, Circuit Judge.

This appeal is from the decision of the Patent and Trademark Office (PTO) Board of Patent Appeals and Interferences (board) affirming the rejection of all remaining claims in appellant's application for a patent, serial No. 188,735, entitled "Immunoassay Utilizing Monoclonal High Affinity IgM Antibodies," which was filed September 19, 1980. n1 The rejection under 35 U.S.C. § 112, first paragraph, is based on the grounds that appellant's written specification would not enable **[**2]** a person skilled in the art to make the monoclonal antibodies that are needed to practice the claimed invention without undue experimentation. We reverse.

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n1 *In re Wands*, Appeal No. 673-76 (Bd. Pat. App. & Int. Dec. 30, 1986).

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I. *Issue*

The only issue on appeal is whether the board erred, as a matter of law, by sustaining the examiner's rejection for lack of enablement under 35 U.S.C. § 112, first paragraph, of all remaining claims in appellants' patent application, serial No. 188,735.

II. *Background*

A. *The Art.*

The claimed invention involves immunoassay methods for the detection of hepatitis B surface antigen by using high-affinity monoclonal antibodies of the IgM isotype. *Antibodies* are a class of proteins (immunoglobulins) that help defend the body against invaders such as viruses and bacteria. An antibody has the potential to bind tightly to another molecule, which molecule is called an *antigen*. The body has the ability to make millions of **[**3]** different antibodies that bind to different antigens. However, it is only after exposure to an antigen that a complicated *immune response* leads to the production of antibodies against that antigen. For example, on the surface of hepatitis B virus particles there is a large protein called *hepatitis B surface antigen* (HBsAg). As its name implies, it is capable of serving as an antigen. During a hepatitis B infection (or when purified HBsAg is injected experimentally), the body begins to make antibodies that bind tightly and specifically to HBsAg. Such antibodies can be used as reagents for sensitive diagnostic tests (*e.g.*, to detect hepatitis B virus in blood and other tissues, a purpose of the claimed invention). A method for detecting or measuring antigens by using antibodies as reagents is called an *immunoassay*.

Normally, many different antibodies are produced against each antigen. One reason for this diversity is that different antibodies are produced that bind to different regions (determinants) of a large antigen molecule such as HBsAg. In addition, different antibodies may be produced that bind to the same determinant. These usually differ in the tightness with **[**4]** which they bind to the determinant. *Affinity* is a quantitative measure of the strength of antibody-antigen binding. Usually an antibody with a higher affinity for an antigen will be more useful for immunological diagnostic tests than one with a lower affinity. Another source of heterogeneity is that there are several immunoglobulin classes or *isotypes*. Immunoglobulin G (IgG) is the most common isotype in serum. Another isotype, immunoglobulin M (IgM), is prominent early in the immune response. IgM molecules are larger than IgG molecules, and have 10 antigen-binding sites instead of the 2 that are present in IgG. Most immunoassay methods use IgG, but the claimed invention uses only IgM antibodies.

For commercial applications there are many disadvantages to using antibodies from serum. Serum contains a complex mixture of antibodies against the antigen of interest within a much larger pool of antibodies directed at other antigens. These are available only in a limited supply that ends when the donor dies. The goal of monoclonal antibody technology is to produce an unlimited supply of a single purified antibody.

The blood cells that make antibodies are *lymphocytes*. Each **[**5]** lymphocyte makes only one kind of antibody. During an immune response, lymphocytes exposed to **[*734]** their particular antigen divide and mature. Each produces a *clone* of identical daughter cells, all of which secrete the same antibody. Clones of lymphocytes, all derived from a single lymphocyte, could provide a source of a single homogeneous antibody. However, lymphocytes do not survive for long outside of the body in cell culture.

Hybridoma technology provides a way to obtain large numbers of cells that all produce the same antibody. This method takes advantage of the properties of *myeloma* cells derived from a tumor of the immune system. The cancerous myeloma cells can divide indefinitely in vitro. They also have the potential ability to secrete antibodies. By appropriate experimental manipulations, a myeloma cell can be made to fuse with a lymphocyte to produce a single hybrid cell (hence, a hybridoma) that contains the genetic material of both cells. The hybridoma secretes the same antibody that was made by its parent lymphocyte, but acquires the capability of the myeloma cell to divide and grow indefinitely in cell culture. Antibodies produced by a clone of hybridoma **[**6]** cells (i.e., by hybridoma cells that are all progeny of a single cell) are called monoclonal antibodies. n2

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n2 For a concise description of monoclonal antibodies and their use in immunoassay see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1368-71, 231 USPQ 81, 82-83 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947, 107 S. Ct. 1606, 94 L. Ed. 2d 792 (1987).

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B. *The Claimed Invention.*

The claimed invention involves methods for the immunoassay of HBsAg by using high-affinity monoclonal IgM antibodies. Jack R. Wands and Vincent R. Zurawski, Jr., two of the three coinventors of the present application, disclosed methods for producing monoclonal antibodies against HBsAg in United States patent No. 4,271,145 (the '145 patent), entitled "Process for Producing Antibodies to Hepatitis Virus and Cell Lines Therefor," which patent issued on June 2, 1981. The '145 patent is incorporated by reference into the application on appeal. The specification of the **[**7]** '145 patent teaches a procedure for immunizing mice

against HBsAg, and the use of lymphocytes from these mice to produce hybridomas that secrete monoclonal antibodies specific for HBsAg. The '145 patent discloses that this procedure yields both IgG and IgM antibodies with high-affinity binding to HBsAg. For the stated purpose of complying with the best mode requirement of 35 U.S.C. § 112, first paragraph, a hybridoma cell line that secretes IgM antibodies against HBsAg (the 1F8 cell line) was deposited at the American Type Culture Collection, a recognized cell depository, and became available to the public when the '145 patent issued.

The application on appeal claims methods for immunoassay of HBsAg using monoclonal antibodies such as those described in the '145 patent. Most immunoassay methods have used monoclonal antibodies of the IgG isotype. IgM antibodies were disfavored in the prior art because of their sensitivity to reducing agents and their tendency to self-aggregate and precipitate. Appellants found that their monoclonal IgM antibodies could be used for immunoassay of HbsAg with unexpectedly high sensitivity and specificity. Claims 1, 3, 7, **[**8]** 8, 14, and 15 are drawn to methods for the immunoassay of HBsAg using high-affinity IgM monoclonal antibodies. Claims 19 and 25-27 are for chemically modified (*e.g.*, radioactively labeled) monoclonal IgM antibodies used in the assays. The broadest method claim reads:

> 1. An immunoassay method utilizing an antibody to assay for a substance comprising hepatitis B-surface antigen (HBsAg) determinants which comprises the steps of:
>
> contacting a test sample containing said substance comprising HBsAg determinants with said antibody; and
>
> determining the presence of said substance in said sample;
>
> wherein said antibody is a monoclonal high affinity IgM antibody having a binding affinity constant for said HBsAg determinants of at least 10<9> M<-1>.

Certain claims were rejected under 35 U.S.C. § 103; these rejections have not **[*735]** been appealed. Remaining claims 1, 3, 7, 8, 14, 15, 19, and 25-27 were rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the disclosure would not enable a person skilled in the art to make and use the invention without undue experimentation. The rejection is directed solely **[**9]** to whether the specification enables one skilled in the art to make the monoclonal antibodies that are needed to practice the invention. The position of the PTO is that data presented by Wands show that the production of high-affinity IgM anti-HBsAg antibodies is unpredictable and unreliable, so that it would require undue experimentation for one skilled in the art to make the antibodies.

III. *Analysis*

A. *Enablement by Deposit of Microorganisms and Cell Lines.*

The first paragraph of 35 U.S.C. § 112 requires that the specification of a patent must enable a person skilled in the art to make and use the claimed invention. "Patents * * * are written to enable those skilled in the art to practice the invention." n3 A patent need not disclose what is well known in the art. n4 Although we review underlying facts found by the board under a "clearly erroneous" standard, n5 we review **[**10]** enablement as a question of law. n6

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n3 W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 1556, 220 USPQ 303, 315 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851, 105 S. Ct. 172, 83 L. Ed. 2d 107 (1984).

n4 *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

n5 *Coleman v. Dines*, 754 F.2d 353, 356, 224 USPQ 857, 859 (Fed. Cir. 1985).

n6 *Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 1268, 229 USPQ 805, 810 (Fed. Cir. 1986), *cert. denied*, 479 U.S. 1030, 107 S. Ct. 875, 93 L. Ed. 2d 829 (1987); *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960 n.6, 220 USPQ 592, 599 n.6 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 835, 83 L. Ed. 2d 69, 105 S. Ct. 127 (1984).

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Where an invention depends on the use of living materials such as microorganisms or cultured cells, it may be impossible **[**11]** to enable the public to make the invention (i.e., to obtain these living materials) solely by means of a written disclosure. One means that has been developed for complying with the enablement requirement is to deposit the living materials in cell depositories which will distribute samples to the public who wish to practice the invention after the patent issues. n7 Administrative guidelines and judicial decisions have clarified the conditions under which a deposit of organisms can satisfy the requirements of section 112. n8 A deposit has been held necessary for enablement where the starting materials (i.e., the living cells used to practice the invention, or cells from which the required cells can be produced) are not readily available to the public. n9 Even when starting materials are available, a deposit has been necessary where it would require undue experimentation to make the cells of the invention from the starting materials. n10

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N7 *In re Argoudelis*, 58 C.C.P.A. 769, 434 F.2d 1390, 1392-93, 168 USPQ 99, 101-02 (CCPA 1970).

n8 *In re Lundak*, 773 F.2d 1216, 227 USPQ 90 (Fed. Cir. 1985); *Feldman v. Aunstrup*, 517 F.2d 1351, 186 USPQ 108 (CCPA 1975), *cert. denied*, 424 U.S. 912, 47 L. Ed. 2d 316, 96 S. Ct. 1109 (1976); Manual of Patent Examining Procedure (MPEP) 608.01(p)(C) (5th ed. 1983, rev. 1987). *See generally* Hampar, *Patenting of Recombinant DNA Technology: The Deposit Requirement*, 67 J. Pat. Trademark Off. Soc'y 569 (1985). **[**12]**

n9 *In re Jackson*, 217 USPQ 804, 807-08 (Bd. App. 1982) (strains of a newly discovered species of bacteria isolated from nature); *Feldman*, 517 F.2d 1351, 186 USPQ 108 (uncommon fungus isolated from nature); *In re Argoudelis*, 434 F.2d at 1392, 168 USPQ at 102 (novel strain of antibiotic-producing microorganism isolated from nature); *In re Kropp*, 143 USPQ 148, 152 (Bd. App. 1959) (newly discovered microorganism isolated from soil).

n10 *In re Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986) (genetically engineered bacteria where the specification provided insufficient information about the amount of time and effort required); *In re Lundak*, 773 F.2d 1216, 227 USPQ 90 (unique cell line produced from another cell line by mutagenesis).

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In addition to satisfying the enablement requirement, deposit of organisms also can be used to establish the filing date of the application as the prima facie date of invention, n11

[*736] and to satisfy the requirement under 35 U.S.C. § 114 **[**13]** that the PTO be guaranteed access to the invention during pendency of the application. n12 Although a deposit may serve these purposes, we recognized, in *In re Lundak*, n13 that these purposes, nevertheless, may be met in ways other than by making a deposit.

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n11 *In re Lundak*, 773 F.2d at 1222, 227 USPQ at 95-96; *In re Feldman*, 517 F.2d at 1355, 186 USPQ at 113; *In re Argoudelis*, 434 F.2d at 1394-96, 168 USPQ at 103-04 (Baldwin, J. concurring).

n12 *In re Lundak*, 773 F.2d at 1222, 227 USPQ at 95-96; *In re Feldman*, 517 F.2d at 1354, 186 USPQ at 112.

n13 *In re Lundak*, 773 F.2d at 1222, 227 USPQ at 95-96.

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A deposit also may satisfy the best mode requirement of section 112, first paragraph, and it is for this reason that the 1F8 hybridoma was deposited in connection with the '145 patent and the current application. Wands does not challenge the statements by the examiner to the effect that, **[**14]** although the deposited 1F8 line enables the public to perform immunoassays with antibodies produced by that single hybridoma, the deposit does not enable the generic claims that are on appeal. The examiner rejected the claims on the grounds that the written disclosure was not enabling and that the deposit was inadequate. Since we hold that the written disclosure fully enables the claimed invention, we need not reach the question of the adequacy of deposits.

B. *Undue Experimentation.*

Although inventions involving microorganisms or other living cells often can be enabled by a deposit, n14 a deposit is not always necessary to satisfy the enablement requirement. n15 No deposit is necessary if the biological organisms can be obtained from readily available sources or derived from readily available starting materials through routine screening that does not require undue experimentation. n16 Whether the specification in an application involving living cells (here, hybridomas) is enabled without **[**15]** a deposit must be decided on the facts of the particular case. n17

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n14 *In re Argoudelis*, 434 F.2d at 1393, 168 USPQ at 102.

n15 *Tabuchi v. Nubel*, 559 F.2d 1183, 194 USPQ 521 (CCPA 1977).

n16 *Id.* at 1186-87, 194 USPQ at 525; *Merck & Co. v. Chase Chem. Co.*, 273 F. Supp. 68, 77, 155 USPQ 139, 146 (D.N.J. 1967); *Guaranty Trust Co. v. Union Solvents Corp.*, 54 F.2d 400, 403-06, 12 U.S.P.Q. (BNA) 47, 50-53 (D. Del. 1931), *aff'd*, 61 F.2d 1041, 15 U.S.P.Q. (BNA) 237 (3d Cir. 1932), *cert. denied*, 288 U.S. 614, 77 L. Ed. 987, 53 S. Ct. 405 (1933); MPEP 608.01(p)(C) ("No problem exists when the microorganisms used are known and readily available to the public.").

n17 *In re Jackson*, 217 USPQ at 807; *see In re Metcalfe*, 56 C.C.P.A. 1191, 410 F.2d 1378, 1382, 161 USPQ 789, 792 (CCPA 1969).

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Appellants contend that their written specification fully **[**16]** enables the practice of their claimed invention because the monoclonal antibodies needed to perform the immunoassays can be made from readily available starting materials using methods that are well known in the monoclonal antibody art. Wands states that application of these methods to make high-affinity IgM anti-HBsAg antibodies requires only routine screening, and that does not amount to undue experimentation. There is no challenge to their contention that the starting materials (i.e., mice, HBsAg antigen, and myeloma cells) are available to the public. The PTO concedes that the methods used to prepare hybridomas and to screen them for high-affinity IgM antibodies against HBsAg were either well known in the monoclonal antibody art or adequately disclosed in the '145 patent and in the current application. This is consistent with this court's recognition with respect to another patent application that methods for obtaining and screening monoclonal antibodies were well known in 1980. n18 The sole issue is whether, in this particular case, it would require undue experimentation to produce high-affinity IgM monoclonal antibodies.

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n18 *Hybritech*, 802 F.2d at 1384, 231 USPQ at 94.

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Enablement is not precluded by the necessity for some experimentation such as **[*737]** routine screening. n19 However, experimentation needed to practice the invention must not be undue experimentation. n20 "The key word is 'undue,' not 'experimentation.'" n21

> The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. *Ansul Co. v. Uniroyal, Inc.* [448 F.2d 872, 878-79; 169 USPQ 759, 762-63 (2d Cir. 1971), *cert. denied*, 404 U.S. 1018, 30 L. Ed. 2d 666, 92 S. Ct. 680 (1972)]. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed * * *. n22

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n19 *Id.*; *Atlas Powder Co. v. E.I. DuPont De Nemours & Co.*, 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984); *In re Angstadt*, 537 F.2d at 502-504, 190 USPQ at 218; *In re Geerdes*, 491 F.2d 1260, 1265, 180 USPQ 789, 793 (CCPA 1974); *Minerals Separation, Ltd. v. Hyde*, 242 U.S. 261, 270-71, 61 L. Ed. 286, 37 S. Ct. 82 (1916). **[**18]**

n20 *Hybritech*, 802 F.2d at 1384, 231 USPQ at 94; *W.L. Gore*, 721 F.2d at 1557, 220 USPQ at 316; *In re Colianni*, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977) (Miller, J., concurring).

n21 *In re Angstadt*, 537 F.2d at 504, 190 USPQ at 219.

n22 *In re Jackson*, 217 USPQ at 807.

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The term "undue experimentation" does not appear in the statute, but it is well established that enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. n23 Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations. The board concluded that undue experimentation would be needed to practice the invention on the basis of experimental data presented by Wands. These data are not in dispute. However, Wands and the board disagree strongly on the conclusion that **[**19]** should be drawn from that data.

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n23 *See* Hybritech, 802 F.2d at 1384, 231 USPQ at 94; *Atlas Powder*, 750 F.2d at 1576, 224 USPQ at 413.

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Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *In re Forman*. n24 They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. n25

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n24 *In re Forman*, 230 USPQ at 547.

n25 *Id.; see In re Colianni*, 561 F.2d at 224, 195 USPQ at 153 (Miller, J., concurring); *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 577, 146 USPQ 218, 221 (CCPA 1965).

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In order to understand whether the rejection was proper, it is necessary to discuss further the methods for making specific monoclonal antibodies. The first step for making monoclonal antibodies is to immunize an animal. The '145 patent provides a detailed description of procedures for immunizing a specific strain of mice against HBsAg. Next the spleen, an organ rich in lymphocytes, is removed and the lymphocytes are separated from the other spleen cells. The lymphocytes are mixed with myeloma cells, and the mixture is treated to cause a few of the cells to fuse with each other. Hybridoma cells that secrete the desired antibodies then must be isolated from the enormous number of other cells in the mixture. This is done through a series of screening procedures.

The first step is to separate the hybridoma cells from unfused lymphocytes and myeloma cells. The cells are cultured in a medium in which all the lymphocytes and myeloma cells die, and only the hybridoma cells survive. The next step is to isolate and clone hybridomas that make antibodies **[*738]** that bind to the antigen of interest. Single hybridoma cells are placed in separate chambers and are allowed to grow and divide. **[**21]** After there are enough cells in the clone to produce sufficient quantities of antibody to analyze, the antibody is assayed to determine whether it binds to the antigen. Generally, antibodies from many clones do not bind the antigen, and these clones are discarded. However, by screening enough clones (often hundreds at a time), hybridomas may be found that secrete antibodies against the antigen of interest.

Wands used a commercially available radioimmunoassay kit to screen clones for cells that produce antibodies directed against HBsAg. In this assay the amount of radioactivity bound gives some indication of the strength of the antibody-antigen binding, but does not yield a

numerical affinity constant, which must be measured using the more laborious Scatchard analysis. In order to determine which anti-HBsAg antibodies satisfy all of the limitations of appellants' claims, the antibodies require further screening to select those which have an IgM isotype and have a binding affinity constant of at least 10<9 M<-1>. n26 The PTO does not question that the screening techniques used by Wands were well known in the monoclonal antibody art.

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n26 The examiner, the board, and Wands all point out that, technically, the strength of antibody-HBsAg binding is measured as *avidity*, which takes into account multiple determinants on the HBsAg molecule, rather than affinity. Nevertheless, despite this correction, all parties then continued to use the term "affinity." We will use the terminology of the parties. Following the usage of the parties, we will also use the term "high-affinity" as essentially synonymous with "having a binding affinity constant of at least 10<9> M<-1>."

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During prosecution Wands submitted a declaration under 37 C.F.R. § 1.132 providing information about all of the hybridomas that appellants had produced before filing the patent application. The first four fusions were unsuccessful and produced no hybridomas. The next six fusion experiments all produced hybridomas that made antibodies specific for HBsAg. Antibodies that bound at least 10,000 cpm in the commercial radioimmunoassay were classified as "high binders." Using this criterion, 143 high-binding hybridomas were obtained. In the declaration, Wands stated that n27

> It is generally accepted in the art that, among those antibodies which are binders with 50,000 cpm or higher, there is a very high likelihood that high affinity (Ka [greater than] 10<9> M<-1>) antibodies will be found. However, high affinity antibodies can also be found among high binders of between 10,000 and 50,000, as is clearly demonstrated in the Table.

The PTO has not challenged this statement.

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n27 A table in the declaration presented the binding data for antibodies from every cell line. Values ranged from 13,867 to 125,204 cpm, and a substantial proportion of the antibodies showed binding greater than 50,000 cpm. In confirmation of Dr. Wand's statement, two antibodies with binding less than 25,000 cpm were found to have affinity constants greater than 10<9> M<-1>.

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The declaration stated that a few of the high-binding monoclonal antibodies from two fusions were chosen for further screening. The remainder of the antibodies and the hybridomas that produced them were saved by freezing. Only nine antibodies were subjected to further analysis. Four (three from one fusion and one from another fusion) fell within the claims, that is, were IgM antibodies and had a binding affinity constant of at least 10<9> M<-1>. Of the remaining five antibodies, three were found to be IgG, while the other two were IgM for which the affinity constants were not measured (although both showed binding well above 50,000 cpm).

Apparently none of the frozen cell lines received any further analysis. The declaration explains that after useful high-affinity IgM monoclonal antibodies to HBsAg had been found, it was considered unnecessary to return to the stored antibodies to screen for more IgMs. Wands says that the existence of the stored hybridomas was disclosed to the PTO to comply with the requirement under 37 C.F.R. § 1.56 that applicants fully disclose all of their relevant **[*739]** data, and not just favorable results. n28 How these stored hybridomas are viewed **[**24]** is central to the positions of the parties.

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n28 *See* *Rohm & Haas Co. v. Crystal Chem. Co.*, 722 F.2d 1556, 220 USPQ 289 (Fed. Cir. 1983).

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The position of the board emphasizes the fact that since the stored cell lines were not completely tested, there is no proof that any of them are IgM antibodies with a binding affinity constant of at least 10<9> M<-1>. Thus, only 4 out of 143 hybridomas, or 2.8 percent, were *proved* to fall within the claims. Furthermore, antibodies that were proved to be high-affinity IgM came from only 2 of 10 fusion experiments. These statistics are viewed by the board as evidence that appellants' methods were not predictable or reproducible. The board concludes that Wands' low rate of demonstrated success shows that a person skilled in the art would have to engage in undue experimentation in order to make antibodies that fall within the claims.

Wands views the data quite differently. Only nine hybridomas were actually analyzed beyond the initial screening for HBsAg **[**25]** binding. Of these, four produced antibodies that fell within the claims, a respectable 44 percent rate of success. (Furthermore, since the two additional IgM antibodies for which the affinity constants were never measured showed binding in excess of 50,000 cpm, it is likely that these also fall within the claims.) Wands argues that the remaining 134 unanalyzed, stored cell lines should not be written off as failures. Instead, if anything, they represent partial success. Each of the stored hybridomas had been shown to produce a high-binding antibody specific for HBsAg. Many of these antibodies showed binding above 50,000 cpm and are thus highly likely to have a binding affinity constant of at least 10<9> M<-1>. Extrapolating from the nine hybridomas that were screened for isotype (and from what is well known in the monoclonal antibody art about isotype frequency), it is reasonable to assume that the stored cells include some that produce IgM. Thus, if the 134 incompletely analyzed cell lines are considered at all, they provide some support (albeit without rigorous proof) to the view that hybridomas falling within the claims are not so rare that undue experimentation would be needed **[**26]** to make them.

The first four fusion attempts were failures, while high-binding antibodies were produced in the next six fusions. Appellants contend that the initial failures occurred because they had not yet learned to fuse cells successfully. Once they became skilled in the art, they invariably obtained numerous hybridomas that made high-binding antibodies against HBsAg and, in each fusion where they determined isotype and binding affinity they obtained hybridomas that fell within the claims.

Wands also submitted a second declaration under 37 C.F.R. § 1.132 stating that after the patent application was submitted they performed an eleventh fusion experiment and obtained another hybridoma that made a high-affinity IgM anti-HBsAg antibody. No information was provided about the number of clones screened in that experiment. The board determined that, because there was no indication as to the number of hybridomas screened, this declaration had very little value. While we agree that it would have been preferable if Wands had included this information, the declaration does show that when appellants

repeated their procedures they again obtained a hybridoma that produced an antibody that **[**27]** fit all of the limitations of their claims.

We conclude that the board's interpretation of the data is erroneous. It is strained and unduly harsh to classify the stored cell lines (each of which was proved to make high-binding antibodies against HBsAg) as failures demonstrating that Wands' methods are unpredictable or unreliable. n29 At worst, they prove nothing at all about the probability of success, and merely show **[*740]** that appellants were prudent in not discarding cells that might someday prove useful. At best, they show that high-binding antibodies, the starting materials for IgM screening and Scatchard analysis, can be produced in large numbers. The PTO's position leads to the absurd conclusion that the more hybridomas an applicant makes and saves without testing, the less predictable the applicant's results become. Furthermore, Wands' explanation that the first four attempts at cell fusion failed only because they had not yet learned to perform fusions properly is reasonable in view of the fact that the next six fusions were all successful. The record indicates that cell fusion is a technique that is well known to those of ordinary skill in the monoclonal antibody **[**28]** art, and there has been no claim that the fusion step should be more difficult or unreliable where the antigen is HBsAg than it would be for other antigens.

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n29 Even if we were to accept the PTO's 2.8% success rate, we would not be required to reach a conclusion of undue experimentation. Such a determination must be made in view of the circumstances of each case and cannot be made solely by reference to a particular numerical cutoff.

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When Wands' data is interpreted in a reasonable manner, analysis considering the factors enumerated in *In re Forman* leads to the conclusion that undue experimentation would not be required to practice the invention. Wands' disclosure provides considerable direction and guidance on how to practice their invention and presents working examples. There was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known.

The nature of monoclonal antibody technology is that it involves screening **[**29]** hybridomas to determine which ones secrete antibody with desired characteristics. Practitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody. No evidence was presented by either party on how many hybridomas would be viewed by those in the art as requiring undue experimentation to screen. However, it seems unlikely that undue experimentation would be defined in terms of the number of hybridomas that were never screened. Furthermore, in the monoclonal antibody art it appears that an "experiment" is not simply the screening of a single hybridoma, but is rather the entire attempt to make a monoclonal antibody against a particular antigen. This process entails immunizing animals, fusing lymphocytes from the immunized animals with myeloma cells to make hybridomas, cloning the hybridomas, and screening the antibodies produced by the hybridomas for the desired characteristics. Wands carried out this entire procedure three times, and was successful each time in making at least one antibody that satisfied all of the claim limitations. Reasonably interpreted, Wands' record indicates that, in the production of high-affinity IgM antibodies **[**30]** against HBsAG, the amount of effort needed to obtain such antibodies is not excessive. Wands' evidence thus effectively rebuts the examiner's challenge to the enablement of their disclosure. n30

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n30 *In re Strahilevitz*, 668 F.2d 1229, 1232, 212 USPQ 561, 563 (CCPA 1982).

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IV. *Conclusion*

Considering all of the factors, we conclude that it would not require undue experimentation to obtain antibodies needed to practice the claimed invention. Accordingly, the rejection of Wands' claims for lack of enablement under 35 U.S.C. § 112, first paragraph, is reversed.

REVERSED

CONCURBY: NEWMAN (In Part)

DISSENTBY: NEWMAN (In Part)

DISSENT: NEWMAN, Circuit Judge, concurring in part, dissenting in part.

A

I concur in the court's holding that additional samples of hybridoma cell lines that produce these high-affinity IgM monoclonal antibodies need not be deposited. This invention, as described by Wands, is not a selection of a few rare cells from many possible cells. To the contrary, **[**31]** Wands states that all monoclonally produced IgM antibodies to hepatitis B surface antigen have the desired high avidity and other favorable properties, and that all are readily preparable by now-standard techniques.

Wands states that his United States Patent No. 4,271,145 describes fully operable techniques, and is distinguished from his **[*741]** first four failed experiments that are referred to in the Rule 132 affidavit. Wands argues that these biotechnological mechanisms are relatively well understood and that the preparations can be routinely duplicated by those of skill in this art, as in *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947, 107 S. Ct. 1606, 94 L. Ed. 2d 792 (1987). I agree that it is not necessary that there be a deposit of multiple exemplars of a cell system that is readily reproduced by known, specifically identified techniques.

B

I would affirm the board's holding that Wands has not complied with 35 U.S.C. § 112, first paragraph, in that he has not provided data sufficient to support the breadth of his generic **[**32]** claims. Wands' claims on appeal include the following:

> 19. Monoclonal high affinity IgM antibodies immunoreactive with HBsAg determinants, wherein said antibodies are coupled to an insoluble solid phase, and wherein the binding affinity constant of said antibodies for said HBsAg determinants is at least 10<9> M<-1>.
> 26. Monoclonal high affinity IgM antibodies immunoreactive with HBsAg determinants wherein said antibodies are detectably labelled.

Wands states that he obtained 143 "high binding monoclonal antibodies of the right specificity" in the successful fusions; although he does not state how they were determined to be high binding or of the right specificity, for Wands also states that only nine of these 143 were tested.

Of these nine, four (three from one fusion and one from another fusion) were found to have the claimed high affinity and to be of the IgM isotype. Wands states that the other five were either of a different isotype or their affinities were not determined. (This latter statement also appears to contradict his statement that all 143 were "high binding".)

Wands argues that a "success rate of four out of nine", or 44.4%, is sufficient to **[**33]** support claims to the entire class. The Commissioner deems the success rate to be four out of 143, or 2.8%; to which Wands responds with statistical analysis as to how unlikely it is that Wands selected the only four out of 143 that worked. Wands did not, however, prove the right point. The question is whether Wands, by testing nine out of 143 (the Commissioner points out that the randomness of the sample was not established), and finding that four out of the nine had the desired properties, has provided sufficient experimental support for the breadth of the requested claims, in the context that "experiments in genetic engineering produce, at best, unpredictable results", quoting from *Ex parte Forman*, 230 USPQ 546, 547 (Bd.Pat.App. and Int. 1986).

The premise of the patent system is that an inventor, having taught the world something it didn't know, is encouraged to make the product available for public and commercial benefit, by governmental grant of the right to exclude others from practice of that which the inventor has disclosed. The boundary defining the excludable subject matter must be carefully set: it must protect the inventor, so that commercial development **[**34]** is encouraged; but the claims must be commensurate with the inventor's contribution. Thus the specification and claims must meet the requirements of 35 U.S.C. § 112. *In re Fisher*, 57 C.C.P.A. 1099, 427 F.2d 833, 839, 166 USPQ 18, 23-24 (CCPA 1970).

As the science of biotechnology matures the need for special accommodation, such as the deposit of cell lines or microorganisms, may diminish; but there remains the body of law and practice on the need for sufficient disclosure, including experimental data when appropriate, that reasonably support the scope of the requested claims. That law relates to the sufficiency of the description of the claimed invention, and if not satisfied by deposit, must independently meet the requirements of Section 112.

Wands is not claiming a particular, specified IgM antibody. He is claiming all such monoclonal antibodies in assay for hepatitis B surface antigen, based on his teaching that such antibodies have uniformly reproducible high avidity, free of the known **[*742]** disadvantages of IgM antibodies such as tendency to precipitate or aggregate. It is incumbent upon Wands to provide reasonable support for **[**35]** the proposed breadth of his claims. I agree with the Commissioner that four exemplars shown to have the desired properties, out of the 143, do not provide adequate support.

Wands argues that the law should not be "harsher" where routine experiments take a long time. However, what Wands is requesting is that the law be less harsh. As illustrated in extensive precedent on the question of how much experimentation is "undue", each case must be determined on its own facts. *See, e.g.*, *W.L. Gore & Assocs., Inc. v. Garlock, Inc.* 721 F.2d 1540, 1557, 220 USPQ 303, 316 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851, 105 S. Ct. 172, 83 L. Ed. 2d 107 (1984); *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 218 (CCPA 1976); *In re Cook*, 58 C.C.P.A. 1049, 439 F.2d 730, 734-35, 169 USPQ 298, 302-03 (CCPA 1971).

The various criteria to be considered in determining whether undue experimentation is required are discussed in, for example, *Fields v. Conover*, 58 C.C.P.A. 1366, 443 F.2d 1386, 170 USPQ 276 (CCPA 1971); *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 USPQ 218 (CCPA 1965); *Ex parte Forman*, 230 USPQ at 547. **[**36]** Wands must provide sufficient data or authority to show that his results are reasonably predictable within the scope of the claimed generic invention, based on experiment and/or scientific theory. In my view he has

not met this burden.